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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/081,309	02/21/2002	Michael Brandt	20859	3846
151 7590 01/03/2007 HOFFMANN-LA ROCHE INC. PATENT LAW DEPARTMENT 340 KINGSLAND STREET NUTLEY, NJ 07110			EXAMINER CHANDRA, GYAN	
			ART UNIT	PAPER NUMBER
			1646	
SHORTENED STATUTORY PERIOD OF RESPONSE		MAIL DATE	DELIVERY MODE	
3 MONTHS		01/03/2007	PAPER	

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

**Office Action Summary**

Application No.

10/081,309

Applicant(s)

BRANDT ET AL.

Examiner

Gyan Chandra

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 27 October 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1 and 3-15 is/are pending in the application.
- 4a) Of the above claim(s) 3, 7 and 9-11 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1, 4-6, 8 and 12-15 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                       | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>10/27/2006</u>  | 6) <input type="checkbox"/> Other: _____                          |

### **DETAILED ACTION**

The amendment filed on 10/27/2006 in response to the Office Action of 7/26/2006 is acknowledged and has been entered.

The IDS filed on 10/27/2006 has been considered.

#### **Status of Application, Amendments, And/Or Claims**

Claim 2 is cancelled. The amendment of claim 1 has been made of record.

Claims 1 and 3-15 are pending.

Claims 3, 7 and 9-11 are withdrawn.

Claims 1, 4-6, 8 and 12-15 are under examination.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

#### ***Response to Arguments***

##### ***Claim Rejections - 35 USC § 103***

Claims 1, 4-6, 8, and 12-13 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Date et al (Oncogene, 17:3045-3054, 1998) in view of Bartley (US Patent No. 5,766,581) for the reasons of record on pg. 3-5 of the office action mailed on 7/26/2006.

Applicants argue that the reference Barley only teaches pegylation of megakaryocyte growth and development factors (MGDFs) and that there is no apparent teaching of peg-modification of any other protein. Applicants cite Mehvar (2000),

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Francis et al (1998) and Reddy (2000) to support that the art of pegylation is unpredictable.

Applicants arguments have been fully considered and they are not persuasive because Bartley et al teach that pegylation has been used in the preparation of therapeutic protein products, for example, Adagen® which is PEGylated adenosine deaminase is approved for treating severe immunodeficiency disease; PEGylated superoxide dismutase for treating head injury; pegylated alpha interferon for treating hepatitis and many more (col. 5, lines30-37). Mehvar (2000) teaches that in general, pegylated proteins result in decreased protein clearance and immunogenicity (pg. 125, introduction). Mehvar teaches that most of the protein polymers retain the pharmacologic activity of the protein, although to a lesser extent than native protein. However, a significant increase in the plasma half-life of the protein more than compensates for any reduction in the pharmacologic affect of the conjugated protein (pg. 125). Reddy teaches, "pegylation is an established process for modifying proteins" and Reddy emphasizes that the key to generating pegylated proteins with important therapeutic action is the optimization of the process to produce a therapeutic drug with the desired pharmacologic characteristics. Reddy teaches that pegylated proteins have enhanced pharmacologic and pharmacodynamic properties compared to unmodified proteins (pg. 919, right column). Francis et al (1998) teach, "pegylation is a well established technique for the modification of therapeutic peptides and proteins" (pg. 2, under title: PEGylation of proteins and peptides). They teach that surprisingly, the pegylation is a single technique that overcomes with many of the pharmacological and

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toxicological problems of proteins and peptides (pg. 2, left column). Thus, Reddy, Mehvar and Francis teach that the pegylation of protein is an established technique and that one skill in the art may need to optimize the pegylation of a specific protein for a desired outcome. Therefore, the rejection is maintained.

Claims 14 and 15 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Date et al and Bartley et al as applied to claims 1-2, 4-6, 8, and 12-13 above, and further in view of and further in view of Veronese et.al. (US Patent 6,528,485) for the reasons of record on pages 5-6 of the office action mailed on 7/26/2006.

Applicants argue that the Veronese reference does not overcome the deficiencies of Date in combination of Bartley. Applicants argue that Veronese does not provide motivation to combine Date and Bartley.

Applicants arguments have been fully considered but they are not persuasive because Veronese et al teach that the PEGylation of a protein results in a mixture of conjugates with different PEG:protein stoichiometries. (col. 2, lines 21-25). They teach that the attachment of PEG with different molecular weight may have enhanced duration of action as compared to the non-pegylated proteins (col. 2, 57-63). Therefore, it would be obvious to purify pegylated proteins that would result in a better bioavailability and pharmacokinetics profile in vivo compared to non pegylated proteins.

Further, in response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642

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F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

***Conclusion***

No claim is allowed.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

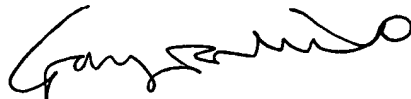
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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gyan Chandra whose telephone number is (571) 272-2922. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol can be reached on (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Art Unit 1646  
19 December 2006  
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